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Fishing for Utility with Expressed Sequences Tags after In re Fisher

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COMMENT

Fishing for Utility with Expressed Sequence Tags After *In re Fisher*

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Abstract

Following the Court of Appeals for the Federal Circuit's decision in In re Fisher *many media reports seemed to imply that patents for expressed sequence tags ("ESTs") were no longer possible. This comment examines the rationale behind the court's decision to deny Fisher a patent for five EST sequences. Section II discusses the history of the utility requirement and its application to* Fisher. *Section III explores the two legal issues that arise from* Fisher, *(1) whether Judge Rader's reasoning in his dissenting opinion should bear any weight in future utility cases for biological inventions; and (2) whether patentable subject matter is still available for ESTs. Section IV proposes that Judge Rader's dissenting opinion should not be employed in future cases. Section IV also proposes that some applications of ESTs can provide limited but substantial and specific utility, thus meeting the Fisher standard.*

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I. INTRODUCTION

Recent media reports covering intellectual property issues in biotechnology seem to imply that patents for the short pieces of DNA called expressed sequence tags ("ESTs") are no longer possible after the Court of Appeals for the Federal Circuit's ("CAFC") September 7, 2005 decision in *In re Fisher*.[1] The *Fisher* court indicated that ESTs seem to have "stumbled at the utility threshold" of patentability.[2] Some of these dire conclusions may be somewhat premature however, echoing Mark Twain's famous response to his premature obituary, "[t]he report of my death was an exaggeration."[3]

Ever since the first attempts to patent ESTs by the National Institutes of Health ("NIH") in the early 1990s, EST patent applications have generated substantial controversy.[4] Some see DNA and therefore ESTs as an unpatentable natural resource, while others desire to protect intellectual property rights in order to reward hard work and costly scientific research efforts.[5] The debate has sparked several proposed solutions including a compulsory licensing system for ESTs[6] and a centralized registration system for ESTs with opportunities for licensing for subsequent research.[7] These proposals recognized the unique problems created with EST patents. That is,

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1. *See Federal Court Rules Gene Fragments Are Not Patentable*, COOLEYALERT! (Cooley Godward LLP, Palo Alto, Cal.), Nov. 2005 (implying by the title of the article that ESTs are unpatentable, but later noting that not all utilities are precluded), *available at* http://www.cooley.com/files/tbl_s24News%5CPDFUpload152%5C1646%5CALERT_GeneFragPatents.pdf. *See also* Phillip B.C. Jones, *ESTs: What Are They Good For?*, ISB NEWS REP. (Va. Tech. U., Blacksburg, Va.), Dec. 2005, at 10 (implying that ESTs are good for "[a]bsolutely nothing"), *available at* http://www.isb.vt.edu/news/2005/artspdf/dec0505.pdf.

2. *See* Paula K. Davis et al., *ESTs Stumble at the Utility Threshold*, 23 NATURE BIOTECHNOLOGY 1227, 1229 (2005) (noting that many present EST applications will not be able to meet the required utility tests and will have to be abandoned).

3. THE OXFORD ESSENTIAL QUOTATIONS DICTIONARY 284 (1998) (appearing originally in the *New York Journal* of June 1897 and commonly misquoted as "Reports of my death have been greatly exaggerated.").

4. Davis, *supra* note 2, at 1227.

5. *See* Molly A. Holman & Stephen R. Munzer, *Intellectual Property Rights in Genes and Gene Fragments: A Registration Solution for Expressed Sequence Tags*, 85 IOWA L. REV. 735, 739-40 (2000) (describing resistance by some parties to the patenting of ESTs).

6. *See generally* Donna M. Gitter, *International Conflicts Over Patenting Human DNA Sequences in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-Use Exemption*, 76 N.Y.U. L. REV. 1623 (2001) (arguing for a compulsory licensing and fair-use exemption structure that would require grantees of DNA sequence patents to license them to commercial researchers).

7. *See generally* Holman & Munzer, *supra* note 5.

how does one protect intellectual property rights but not stymie scientific research on the genes for which the ESTs encode?

Much of the debate stems from the fact that ESTs are only short sequences between 200-800 nucleotides, and generally do not encode for an entire gene sequence.[8] Filing for patent protection on simply a fraction of a gene presents a problem at the utility threshold.[9] If one only has a piece of a gene, how does one elucidate how the gene functions in the body? Additionally, how might it be involved in disease if no research beyond sequencing the EST has been performed? Allowing the right to exclude through granting of a patent is akin to having only a portion of a treasure map and precluding all others from searching for the treasure. Even if another party subsequently can get a hold of a complete copy of the map and easily find the treasure, they would not be allowed to do so.

This comment will examine the rationale behind the court's decision to deny Fisher a patent for five EST sequences for which an application was filed. In Section II, primers on general patent requirements and several areas of molecular biology are presented.[10] Additionally, the section reviews the historical and legal development of patenting biological subject matter.[11] Further, the history of the utility requirement as determined by caselaw,[12] and its application to *Fisher*,[13] is examined in conjunction with Judge Rader's reasons for his dissenting opinion.[14] Section III presents two legal issues that arise from *Fisher*: (1) whether the dissent's line of reasoning should bear any weight in future utility cases for biological inventions; and (2) patentable subject matter still available for ESTs.[15] Section IV proposes that Judge Rader's dissenting opinion should not be employed in future cases, particularly if the Supreme Court decides to rule on the issue of patent utility again. It further proposes that single-nucleotide polymorphism ("SNP") correlations to biological traits and use of ESTs as probes on microarrays are two applications of ESTs

8. *Id.* at 748-49.

9. *In re* Fisher, 421 F.3d 1365, 1368 (Fed. Cir. 2005) (ruling that ESTs that were the subject of a patent application did not meet the utility standard).

10. *See* discussion *infra* Sections II.A–D.

11. *See* discussion *infra* Section II.E.

12. *See* discussion *infra* Section II.F.

13. *See* discussion *infra* Section II.G.

14. *See* discussion *infra* Section II.H.

15. *See* discussion *infra* Section III.

that can provide limited but substantial and specific utility meeting the standards set by the majority in *Fisher*.[16]

II. BACKGROUND

In order to fully understand the issues at hand, one must become familiar with the science and technology central to the *Fisher* case. Additionally, the requirements for patentability regarding biological and biochemical inventions, with a specific focus on the utility requirement, must be understood in light of judicial precedent.

A. Thresholds of Utility

In order to be granted a patent, the inventor must file a patent application with the United States Patent and Trademark Office ("USPTO").[17] The application must be submitted in a timely manner, and contain both a specification that describes the invention and a set of claims that define the boundaries of the invention.[18] Before granting or rejecting a patent application, an examiner at the USPTO examines the patent application to see if it passes the legal patentability requirements including enablement, best mode, clear claims, novelty, non-obviousness, and utility.[19] If it complies with these standards, the patent is granted, allowing the inventor a monopoly for a limited amount of time.[20] The property right granted is the right to exclude others from infringing on the boundaries of the patent's claims, not the right or even the duty to use the patent.[21]

It is the utility requirement that is at the center of the holding in the *Fisher* case.[22] Generally, the standard for utility is that the invention must have a "practical utility."[23] This is usually easily met with inventions in non-biological areas. However, after the Supreme Court's ruling in *Brenner v. Manson*, this standard would prove a substantial bar for biological, chemical, and process claims to chemical inventions because the Court held that such inventions must not simply have a "practical utility," but a "substantial" and "specific"

16. *See* discussion *infra* Section IV.

17. 1 DONALD S. CHISUM, CHISUM ON PATENTS § 1 (2005).

18. *See id.*

19. *Id.*

20. *See id.*

21. *Id.*

22. *See generally* discussion *infra* Section IV.

23. JANICE M. MUELLER, AN INTRODUCTION TO PATENT LAW, 156 (Aspen Publishers 2003).

utility.[24] In the realm of biotechnology, the advent of high-throughput genomic sequencing and the production of EST sequences created significant uncertainty over whether ESTs could meet the standards that had been applied to chemicals and chemical processes.[25]

B. A Primer on Molecular Biology

In order to achieve an understanding of the legal issues in this specific area of patent law, it is essential that one understand the basic dogma of molecular biology. Deoxyribonucleic acid (DNA) is composed of two intertwined chains of polynucleotides that encode an organism's genetic information.[26] Each of these nucleotides, or bases, can be composed of one of four bases: adenine (A), cytosine (C), guanine (G), or thymine (T).[27] A small, but significant component of an organism's DNA encodes for genes while the rest of the DNA can exist as regions that either regulate gene expression, or constitute "selfish" or "junk" DNA.[28] Genes are transcribed, or "copied," into another type of polynucleotide known as ribonucleic acid (RNA), which substitutes the DNA base thymine (T) with uracil (U).[29] The RNA that is transcribed from a gene is called messenger RNA ("mRNA") and is read by ribosome organelles inside the cellular cytoplasm.[30] The mRNA is translated three nucleotides at a time into a protein sequence composed of a chain of amino acids rather than a chain of nucleotides as with DNA and RNA.[31] In most cases, every amino acid residue is composed of 1 of 20 possible amino acids, and the sequence of amino acids determines the sequence and the function of the protein.[32] Proteins function as the workhorses of genes, serving roles as hormones, receptors, intracellular signal transducers, and even as transcribers and translators of DNA and RNA themselves.[33]

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24. *See generally* Brenner v. Manson, 383 U.S. 519 (1966) (ruling that a process to produce a novel steroidal compound failed to cross the substantial and specific utility threshold).

25. MUELLER, *supra* note 23, at 202-04.

26. *See* OXFORD DICTIONARY OF BIOLOGY 193-94 (Elizabeth Martin and Robert S. Hine eds., 5th ed. 2004) (defining "DNA (deoxyribonucleic acid)").

27. *Id.*

28. *See id.* at 581 (defining "selfish DNA").

29. *See id.* at 564-65 (defining "RNA (ribonucleic acid)").

30. *Id.*

31. *Id.*

32. *See id.* at 26-27 (defining "amino acid").

33. *See* Holman & Munzer, *supra* note 5, at 741-42. *See also* OXFORD DICTIONARY OF BIOLOGY, *supra* note 26, at 526-27.

One of the interesting features of different bodily tissues is that they express varying levels of specific genes.[34] For example, pancreatic tissue may express higher levels of the gene for insulin than other bodily tissues.[35] To study differential gene expression, scientists often create "libraries" of genes expressed in different tissues.[36] To do this, they make DNA copies of the RNA expressed in specific tissues called complementary DNA (cDNA) libraries.[37] Of course, having the genes in a cDNA library does not give scientists the actual nucleotide sequences of the genes, so they must sequence the genes contained in the libraries.[38] Technical limitations only allow scientists to sequence short segments of the genes, and these short segments have been commonly designated as expressed sequence tags ("ESTs").[39] ESTs are randomly isolated and only rarely give the full sequence of the gene. But they do allow for some understanding of the sequence of a gene and, perhaps, the ability to identify possible functions of the protein encoded by the gene.[40]

During the mid-to-late 1990's and early 2000's, institutions and companies competed to discover novel genes from different organisms and to achieve patent protection for their discoveries.[41] Monsanto, the company behind the appellants in *Fisher*, analyzed genes from the corn or maize genome for example.[42] These companies faced an interesting dilemma involving the utility requirement for patentability set forth by the United States Patent and Trademark Office (USPTO).[43] After sequencing an EST from a novel gene, does one file for protection immediately, or does one spend substantial time and effort to sequence the entire gene sequence and subsequently apply for patent protection? Further, even if one has the

34. *See* OXFORD DICTIONARY OF BIOLOGY, *supra* note 26, at 648 (defining "transcriptomics").

35. *See id.* at 468-69 (defining "pancreas" and identifying it as a source of insulin production).

36. *See* Holman & Munzer, *supra* note 5, at 748-49.

37. *See id.* at 749-50.

38. *See id.*

39. *Id.* at 749.

40. *Id.*

41. *See* Davis, *supra* note 2, at 1227.

42. *See In re* Fisher, 421 F.3d 1365, 1367-68 (Fed. Cir. 2005) (noting that Fisher's ESTs were derived "from pooled leaf tissue harvested from maize plants . . . .").

43. *See* Holman & Munzer, *supra* note 5, at 750-51 (noting that case law indicated that a whole gene should be sequenced before a patent can be granted and despite this, EST patent applications were attempted).

complete sequence, does one wait until the function of the gene is determined through laboratory research?

On one side of the argument, filing too early may produce an application that will fail the utility requirement for patentability as it did in *Fisher*.[44] On the other hand, waiting until one determines the function of the gene which can take months, even years of research, can allow a competitor to file an application for the gene. This can create prior art that may bar one's ability to be awarded composition of matter claims on the gene. Further, before the ruling in *Fisher*, patent protection for ESTs was a legal uncertainty. Thus, it was conceivable that if a competitor achieved patent protection for an EST, he or she could preclude others from working on and commercializing a gene product.[45] This may explain why some companies gambled and filed patent applications for ESTs rather than entire genes.

One step towards answering these questions is to ask for what will the gene be used. The genetic information provided by genes can be used therapeutically and/or commercially in several ways: (1) as a biotherapeutic itself using the encoded protein;[46] (2) as a target for small molecule or antibody-based therapeutics;[47] or (3) as a diagnostic marker for certain biological traits.[48] It is the diagnostic marker example where ESTs can most likely meet the utility requirement required by the USPTO.

C. Single Nucleotide Polymorphisms ("SNPs")

One of the uses of the ESTs claimed by Fisher was for identifying single nucleotide polymorphisms in the gene.[49] Therefore, to understand the case, it is essential to be acquainted with single

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44. *See* discussion *infra* Section II.G.

45. *See id.* (noting that it was prudent for the NIH to file for patent protection on its EST sequences because of the uncertainty of rights that might be bestowed on the inventions).

46. Proteins derived from genes are sometimes produced artificially as pharmaceutical agents themselves. Two common examples are insulin and erythropoietin.

47. A good example is vascular endothelial growth factor, which has been targeted by a humanized antibody called Avastatin and produced by Genentech for treatment of colon and rectal cancers. Genentech, http://www.gene.com/gene/pipeline/status/oncology/avastin/index.jsp (last visited Jan. 14, 2007).

48. *See* Jeanette J. McCarthy & Rolf Hilfiker, *The Use of Single-Nucleotide Polymorphism Maps in Pharmacogenomics*, 18 NATURE BIOTECHNOLOGY 505 (2000) (noting that genetic markers in the form of polymorphisms have been correlated with diseases such as deep-vein thrombosis and HIV infection susceptibility).

49. *In re* Fisher, 421 F.3d 1365, 1368 (Fed. Cir. 2005)

nucleotide polymorphisms and their application to the detection and treatment of disease.

Single nucleotide polymorphisms ("SNPs") are a common type of genetic variation.[50] As the name implies, they are regions of DNA where one nucleotide base is substituted for another, creating a mutation in a subpopulation of a species.[51] If a SNP occurs within the coding region of a gene, there are two possible effects on the protein encoded by the gene. First, because of the degeneracy of the genetic code, it actually may be a silent mutation, and leave the protein unaffected.[52] The other alternative is that a mutation may cause a change in the protein sequence itself, which can significantly affect its function, as illustrated in sickle-cell anemia when the amino acid glutamate is replaced by valine.[53]

It is the quest of scientists in the pharmacogenetics field to catalog SNPs, and to analyze their frequencies of occurrence in different populations of species, particularly those that have a higher prevalence of a certain disease.[54] Further, they hope to understand how these variations affect a certain population's response to drug therapy because some populations with certain SNPs or combinations of SNPs either can or cannot respond to such therapies or suffer serious adverse effects upon treatment.[55] If a SNP can predict the response, then it is the goal of researchers to tailor pharmaceutical therapy according to a person's likelihood of responding, rather than simply treating someone according to how the entire population is likely to respond.[56]

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50. *See* OXFORD DICTIONARY OF BIOLOGY, *supra* note 26, at 592 (defining single nucleotide polymorphism and stating that one must be present in at least 1% of the population).

51. *Id.*

52. RNA is read three nucleotides at a time, with the three nucleotides termed a "codon." Because there are 64 possible three-nucleotide combinations, and only 20 possible amino acids, some codons are redundant, forming a "degenerate" code. JAMES D. WATSON ET AL., RECOMBINANT DNA 41 (2d ed. 1992).

53. *Id.* at 33.

54. *See* Allen D. Roses, *Genome-Based Pharmacogenetics and the Pharmaceutical Industry*, 1 NATURE REVIEWS DRUG DISCOVERY 541 (2002).

55. *See id.* at 544-45 (showing a significant correlation between a genetic marker and an adverse response to the drug Tranilast in a Phase III clinical trial).

56. *See id.* at 544 ("[A] standard SNP genetic-profiling system can be forseen for targeting effective medicines to responsive patients, as well as predicting which individuals carry genetic risk factors for [adverse events].").

D. Gene Expression Using Microarray Technology

Another use asserted by Fisher was for "measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression."[57] Microarrays are a relatively recent technology capable of producing information about the expression of thousands of genes in a tissue.[58] They consist of a surface, usually a slide or a bead, on which thousands of DNA molecules of known sequence are linked.[59] The DNA that is linked to the surface can itself be an EST sequence or a set of smaller DNA molecules (oligonucleotides) that represent an EST or a full-length gene.[60]

RNA from a tissue is converted into thousands of labeled probes, which bind the DNA on the slide it matches the RNA sequence.[61] In this manner, the intensity of binding quantifies how much each of the thousands of genes on the microarray surface is expressed in the specific tissue being tested. One common result from such experiments is the discovery of genes that are highly expressed in cancer tissues, but not normal tissue, creating hypotheses about genes and proteins that might be responsible for cancer progression.[62]

E. The Legal Development of Gene Patents

During the past sixty years, patents on biological material have undergone much development. In 1948, the "products of nature" doctrine was in full force, and the Supreme Court in *Funk Bros. Seed Co. v. Kalo Inoculant Co.* used the doctrine to invalidate a patent by a bacterial inoculant company.[63] The invention was a mixture of 6 species of *Rhizobium* bacteria that enabled proper nitrogen-fixing in several agricultural species of plant.[64] Despite the fact that such a mixture comprised a vast improvement over previous inoculants, the Supreme Court found that "[t]he qualities of these bacteria, like the heat of the sun . . . are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and

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57. *In re* Fisher, 421 F.3d 1365, 1368 (Fed. Cir. 2005)

58. *See* OXFORD DICTIONARY OF BIOLOGY, *supra* note 26, at 196 (defining "DNA microarray").

59. *See id.*

60. *See id.*

61. *See id.*

62. *See id.* (implying that microarrays have successfully made a correlation between BRCA gene expression and hereditary forms of breast cancer).

63. Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 128-29 (1948).

64. *Id.*

reserved exclusively to none."[65] Since all six bacteria species were naturally occurring, the Supreme Court found that there could not be a patent on the mixture because they were all products of nature.[66]

In 1980, by contrast, the Supreme Court found that a bacterium was patentable in *Diamond v. Chakrabarty*.[67] Chakrabarty had inserted a plasmid comprised of exogenous DNA into a naturally occurring bacterium, altering it so that it could digest crude oil, and thus be useful in cleaning up oil spills.[68] The "products of nature" doctrine was not applicable in this case because the bacterium was not a naturally occurring organism due to the exogenous DNA inserted into it.[69]

Similarly, the "products of nature" doctrine did not impede attempts to patent biochemical inventions. In *In re Bergstrom*, the Court of Customs and Patent Appeals ("CCPA") held that purified prostaglandins were patentable subject matter, despite the fact that prostaglandins were naturally occurring and thus appeared to fall under the "products of nature" doctrine.[70] The court found that "pure materials necessarily differ from . . . impure materials and, if the latter are the only ones existing and available as a standard of reference, as seems to be the situation here . . . the 'pure' materials are 'new' . . . ."[71]

By 1991 it was evident that DNA and the proteins it encoded were patentable subject matter despite arguably being products of nature.[72] In *Amgen v. Chugai Pharmaceuticals*, the CAFC found genes to be complex chemical compounds.[73] In order to be patentable, inventors must first show how it is different from other genes, and also show how to isolate that gene sequence.[74] Amgen however was not awarded all of the thousands of possible variants of the gene because it did not enable a way to produce all of them in its patent

65. *Id.* at 130.

66. *Id.* at 134-35.

67. Diamond v. Chakrabarty, 447 U.S. 303 (1980).

68. *Id.* at 305 (1980).

69. *See id.* at 313 ("Congress thus recognized that the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions.").

70. In re Bergstrom, 427 F.2d 1394, 1401-02 (C.C.P.A. 1970).

71. *Id.* at 1402.

72. Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1203-04 (Fed. Cir. 1991) (noting that the patent office had issued patents on both the isolated erythropoietin DNA and protein sequences).

73. *Id.* at 1206.

74. *Id.*

specification.[75] But the patenting of human genes now had legal precedent.

In 2005, *Fisher* addressed the question of patentability of ESTs.[76] Unlike in *Amgen v. Chugai*, the DNA sequences implicated in *Fisher* were short, incomplete sequences of genes, not full-length genes encoding for an active protein.[77] Although hailed as a victory against the patenting of ESTs, the CAFC did not broadly hold that ESTs in general were unpatentable. Rather, it held that Fisher's asserted utilities for the ESTs were not supported by the specification, and did not present the substantial or specific utility required.[78]

F. The Utility Requirement and Establishment of the Higher Threshold for Biochemical Discoveries

In the early Nineteenth Century, before the patent office was faced with the intricacies of modern-day inventions, Justice Joseph Story set the initial standard of utility in order to patent an invention.[79] This standard was that an invention had to have some type of beneficial use, and not be detrimental or amoral.[80] Most courts accept this standard today for most fields of technology.[81] However, a higher standard would develop in the Twentieth Century for chemical inventions,[82] which would later be applied to EST inventions.

In 1960, the CCPA in *In re Nelson* allowed claims to a new C-19 14-hydroxy-androstene genus of compounds.[83] The asserted utility of the compounds was as chemical intermediates in the preparation of new, undisclosed steroid compounds. The court found that the utility threshold had been satisfied because the intermediates could be used to make new compounds that were related to steroids with previously demonstrated therapeutic value, and therefore were clearly useful to society.[84] In reversing the patent office's rejection of the applicants' claims, the court said the patent office was wrong in demanding a "practical utility" test.[85]

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75. *Id.* at 1213.
76. *In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005).
77. *See generally* discussion *infra* Section II.G.
78. *See In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005).
79. 1-4 CHISUM, *supra* note 17, § 4.02[1].
80. *Id.*
81. *Id.*
82. *See generally* Brenner v. Manson, 383 U.S. 519 (1966).
83. *In re* Nelson, 280 F.2d 172, 188 (C.C.P.A. 1960).
84. *Id.* at 180-81.
85. *Id.*

However, six years later in *Brenner v. Manson*, the Supreme Court adjusted Justice Story's broad definition of utility, and adopted a substantial and specific standard reminiscent of the practical utility standard rejected in *Nelson*.[86] The applicant in *Brenner* claimed a process to synthesize a novel genus of steroid molecules, and asserted utility based on the fact that steroids with similar, but not exactly the same structures had been shown to inhibit tumor growth.[87] In rejecting the claims, the court held that simply being similar to a compound of known utility did not pass the utility threshold, and the applicant must show that the compound must have a "sufficient likelihood that the steroid yielded by his process would have similar tumor-inhibiting characteristics."[88]

In rejecting Justice Story's broad definition of utility, the court applied a more rigorous standard to process patents in chemistry. Granting a patent for a compound with a hypothetical utility and no indication that the utility has sufficient likelihood of existing "creates a monopoly of knowledge . . . [with] metes and bounds . . . not capable of precise delineation."[89] Thus, the utility advanced in *Brenner* was insufficient because it was an improbable hypothetical. A grant of a patent would violate "[t]he basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly . . . ."[90] So the court held that if the process of making the compound was to pass the utility threshold, it must have both substantial utility, and carry a specific benefit in "currently available form," not a hypothetical one.[91]

Finally, the Court in *Brenner* made the often-quoted statement that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."[92] To the Court, finding a possibly important chemical intermediate without substantial and specific utility was inadequate for a patent grant. This was despite the importance that the subject matter may later prove to be useful in the industry.[93]

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86. *See Brenner*, 383 U.S. 519.
87. *Id.* at 522.
88. *Id.*at 532.
89. *Id.* at 534.
90. *Id.*
91. *Id.* at 534-35.
92. *Id.* at 536.
93. *Id.*

Brenner was the most recent case in which the Supreme Court addressed the subject of the utility requirement in patent law.[94] Since then, lower courts have used *Brenner* as a guideline for interpreting utility requirements, especially in chemical patent cases when the facts of *Brenner* closely parallel those of the case at hand.[95]

The CCPA applied the new standard a year after *Brenner* in another chemical compound case. In *In re Kirk*, the applicant had applied for patent protection on new steroid compounds.[96] As in *Brenner*, the applicant did not know at the time of the application of any specific activity or function possessed by the steroid compounds.[97] An affidavit filed subsequently revealed that the applicant had determined that several of the chemical compounds had progestational, glucocorticoid, or anti-inflammatory activities.[98] However, the court rejected the claims because these activities were not even remotely mentioned in the patent's specification as filed.[99] Therefore, the substantial and specific utility requirements could not be satisfied when knowledge of the compounds' functions were only discovered after the patent application had been filed. Furthermore, creating a chemical compound with a utility only opening a door to further chemical research amounted to the "hunting license" prohibited by the Supreme Court in *Brenner*.[100]

In contrast, in *In re Jolles*, the CCPA allowed claims to a set of novel compounds with no proven function at the time the patent was filed.[101] A subsequently filed declaration by the applicants showed that one of the compounds was effective in treating acute myeloblastic leukemia (AML) in human clinical trials.[102] Another declaration showed that other compound species were effective in

94. MUELLER, *supra* note 23 at 159.

95. *See, e.g.*, *In re* Kirk, 376 F.2d 936, 945-46 (C.C.P.A. 1967) (holding that in certain cases chemical compositions and not just methods of producing them do not pass the utility threshold). *See also* Cross v. Iizuka, 753 F.2d 1040, 1051 (Fed. Cir. 1985) (holding that *in vitro* data produced from the novel compound in conjunction with *in vitro* and *in vivo* data from compounds of similar structure provides sufficient utility).

96. *Kirk*, 376 F.2d at 937.

97. *Id.* at 941 The court noted that "the nebulous expressions 'biological activity' or 'biological properties' appearing in the specification convey no . . . explicit indication of the usefulness of the compounds and how to use them . . . ." *Id.*

98. *Id.* at 939-40.

99. *See id.* at 945 (noting that claimed utilities like "useful in research" and "useful as building blocks of value to the researcher" were too insubstantial and vague).

100. *Id.* at 942.

101. *In re* Jolles, 628 F.2d 1322, 1323-24 (C.C.P.A. 1980).

102. *Id.*

treating AML in laboratory mice.[103] Although allowing the claims here seemed contrary to the ruling in *Kirk*, the key difference was that the applicants in *Jolles* asserted the anti-AML utility in their specification at the time of filing the application.

The court further stated the importance of animal testing, and its relevance to establishing utility for chemical compounds.[104] It also held that the utility threshold can be met if "one of ordinary skill in the art would accept appellant's claimed utility in humans . . . ."[105] Because the applied-for compounds were effective in animal studies and were substantially related to the compound effective in human clinical trials, the court concluded one with skill in the art would recognized the utility.[106]

By the 1980's, lower courts appeared to use the term "practical utility" interchangeably with "substantial" and "specific utility."[107] In *Cross v. Iizuka*, the CAFC held that *in vitro* data disclosed within an application was enough to establish practical utility under certain circumstances.[108] An asserted use for the inhibition of the thromboxane synthetase enzyme supplemented with both *in vitro* data and the fact that structurally similar compounds had similar *in vitro* and *in vivo* effects, passed the practical utility threshold.

The CAFC further explained in *Fujikawa v. Wattanasin* that when appropriate, *in vitro* evidence proffered by the applicant is "the first link in the screening chain . . . [and] may establish a practical utility for the compound in question."[109] If correlated to *in vitro* and *in vivo* results to structurally similar compounds, "[a]ll that is required is that the tests be '*reasonably* indicative of the desired [pharmacological] response.'"[110] One more reason practical utility was satisfied was that the court desired to arm the medical profession "with an arsenal of chemicals having known pharmacological

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103. *Id.* at 1324.

104. *Id.*at 1327.

105. *Id.* at 1327-28.

106. *Id.*

107. Cross v. Iizuka, 753 F.2d 1040, 1046 (Fed. Cir. 1985).

108. *Id.* at 1051 ("Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility.").

109. Fujikawa v. Wattanasin, 93 F.3d 1559, 1565 (Fed. Cir. 1996).

110. *Id.* at 1564 (emphasis in original) (quoting Nelson v. Bowler, 626 F.2d 853, 856 (C.C.P.A. 1980)).

activities."[111] This accelerates and focuses medical research rather than simply leading to undirected research.

G. *Applying the Stricter Standard of Utility to ESTs in* Fisher

In the NIH's efforts to seek patent protection for ESTs, it hoped to obtain protection on the underlying proteins themselves, for which the EST sequences partially coded.[112] Although initiated by the government, private businesses soon followed suit.[113] The NIH eventually abandoned its EST applications, but private companies, like those in the *Fisher* case did not.[114]

In 1999, the USPTO considered drafting new utility guidelines, and solicited public input. Bruce Alberts, President of the National Academy of Sciences, commented:

> [t]hose who would patent human DNA sequences without real knowledge of their utility are staking claims not only to what little they know at the moment, but also to everything that might later be discovered about the genes and proteins associated with the sequence. They are, in effect, laying claim to a function or use that does not yet exist.[115]

The USPTO subsequently set guidelines for the utility requirement in 2001,[116] and *In re Fisher* was the first appeal to reach the CAFC concerning the issue.[117] The court entered its decision on September 7, 2005.[118]

The facts of the case are straightforward. Appellants Dane K. Fisher and Raghunath Lalgudi of Monsanto Technology LLC ("Fisher")[119] appealed the rejection of their patent application by both the USPTO examiner and the USPTO Board of Appeals and Patent Interferences ("BPAI") for failure to show sufficient utility.[120] Fisher had applied for patent protection for thousands of EST sequences derived from pooled leaf tissue of the maize plant.[121] The application

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111. *Id.*

112. Davis, *supra* note 2, at 1227.

113. *Id.*

114. *Id.*

115. *Id.*

116. *See* Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

117. Davis, *supra* note 2, at 1227.

118. *In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005).

119. *Id.* at 1366 n.1 ("The real party in interest is Monsanto Technology, LLC, which is owned by the Monsanto Company.").

120. *Id.* at 1367.

121. *Id.* at 1367-68.

had been restricted to five specific EST sequences and included the following claims:

> (1) serving as a molecular marker for mapping the entire maize genome, which consists of ten chromosomes that collectively encompass roughly 50,000 genes; (2) measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression; (3) providing a source for primers for use in the polymerase chain reaction ("PCR") process to enable rapid and inexpensive duplication of specific genes; (4) identifying the presence or absence of a polymorphism; (5) isolating promoters via chromosome walking; (6) controlling protein expression; and (7) locating genetic molecules of other plants and organisms.[122]

For the appeal, Fisher had elected to assert only the third and fourth claims relating to providing a source for primers, and to identifying the presence or absence of a polymorphism.[123]

In affirming the rejection by the USPTO Board of Patent Appeals and Interferences, the court compared the facts in *Fisher* to those of *Brenner*, decided almost four decades earlier by the Supreme Court.[124] The ESTs were compared to chemical intermediates, and were also analogized to research tools.[125] One reason *Brenner* was used was that the USPTO utility guidelines were not binding upon the court.[126] Therefore, the utility test employed was the substantial and specific utility test from *Brenner*.

The Supreme Court in *Brenner* had not established a specific test for either substantial or specific utility, so the court defined such a test itself in *Fisher*. [127] For an invention to have substantial utility, it "must show that the claimed invention has a significant and presently available benefit to the public."[128] Specific utility, it was held, must provide "an immediate well-defined, real world benefit to the public" and is also required to "disclose a use which is not so vague as to be meaningless."[129]

Despite the fact that the *Fisher* case involved biological subject matter whereas prior cases invoking the utility requirement focused

122. *Id.* at 1368.
123. *Id.*
124. *Id.* at 1374.
125. *Id.* at 1373-74.
126. *Id.* at 1372.
127. *See id.* at 1371.
128. *Id.*
129. *Id.*

on chemistry, the court found no reason to distinguish the two types of inventions.[130] The ESTs in *Fisher* were substantially similar to the process of creating the compounds in *Brenner*. Both inventions laid claim to products of unknown use.[131] The ESTs in *Fisher* simply encoded a part of a gene, and that gene was of completely unknown function according to the specification of the patent application.[132] This was similar to creating novel chemical structures of unknown biochemical function.[133]

The facts of *Kirk* were found to be particularly analogous to the *Fisher* case.[134] The applicant in *Kirk* had asserted his two uses, one for biological activity[135] and the other for use as a chemical intermediate to prepare steroidal compounds.[136] Similarly, the EST sequences claimed by Fisher could only be used "to gain further information about the underlying genes and the proteins encoded for by those genes."[137] They were tools "to be used along the way in the search for a practical utility."[138] These similarities to *Kirk* and *Brenner* made the granting of Fisher's application amount to a "hunting license", relating the patent system to "the realm of philosophy" and not the "world of commerce."[139]

Fisher attempted to draw an analogy between its application and the *Cross* case, but the court found the analogy to be lacking.[140] In *Cross*, specific pharmaceutical uses for inhibition of thromboxane synthetase to stimulate smooth muscle and modulate blood pressure were supported by *in vitro* and *in vivo* data.[141] In contrast, the court noted that Fisher's ESTs were claimed to have a wide variety of uses, none of which was supported by data, either *in vitro* or *in vivo*.[142] The court was especially strident in noting that Fisher had not produced even one identified polymorphism, nor isolated a single gene

130. *Id.* at 1374-75.
131. *Id.* at 1374.
132. *Id.* at 1376.
133. *See id.* at 1374.
134. *Id.* at 1374.
135. *Id.*
136. *Id.* at 1375.
137. *Id.* at 1376.
138. *Id.*
139. *Id.*
140. *Id.* ("Fisher's reliance on *Jolles, Nelson,* and *Cross*, cases which found utility in certain claimed pharmaceutical compounds, is misplaced.").
141. *Id.* at 1377.
142. *See id.*

promoter.[143] In *Cross*, the uses were not "nebulous expressions, such as 'biological activity' or 'biological properties' . . . . [i]nstead, the alleged uses in those cases gave a firm indication of the precise uses to which the claimed compounds could be put."[144]

Finally, Fisher attempted to relate the value that EST databases have in a commercial setting in order to illustrate the value, and therefore the utility of EST sequences.[145] However, once again the court did not accept the argument, stating that "Fisher did not present any evidence showing that agricultural companies have purchased or even expressed any interest in the claimed ESTs."[146] Interestingly though, despite the court holding that Fisher's claimed ESTs had no commercial value, it did reiterate that precedent holds that "commercial success may support the utility of an invention."[147]

H. Judge Rader's Dissent (An EST is Like a Microscope)

The decision from the CAFC was not a unanimous one from the three-judge panel.[148] Judge Rader found that the utility threshold had been met by Fisher, satisfying the utility requirements set forth by Congress in 35 U.S.C. § 101 (2000).[149] He found that the ESTs had a utility as a research tool in revealing information about other molecules such as the DNA from which the ESTs were derived.[150] Further, he cited the USPTO's Manual of Patent Examining Procedure,[151] comparing ESTs to other patentable tools such as gas chromatographs, screening assays, and DNA sequencing tools.[152]

Judge Rader distinguished the lack of utility problems that were mentioned by the majority when they compared *Fisher* to *Brenner* and *Kirk*. He noted that in the preceding cases, a steroidal chemical

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143. *See id.* ("Fisher did not show that even one of the claimed ESTs had been tested and successfully aided in identifying a polymorphism in the maize genome or in isolating a single promoter that could give clues about protein expression.").

144. *Id.* at 1377 (quoting Cross v. Iizuka, 753 F.2d 1040, 1048 (Fed. Cir. 1985)).

145. *See id.* at 1377-78.

146. *Id.* at 1377.

147. *Id.* at 1377-78 (quoting Raytheon Co. v. Roper Corp., 724 F.2d 951, 959 (Fed. Cir. 1983)).

148. *Id.* at 1379 (Rader, J., dissenting).

149. *Id.*

150. *Id.*

151. UNITED STATES PATENT AND TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE § 2107.01 (8th ed. 2006) ("Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility.").

152. *Fisher*, 421 F.3d at 1379 (Rader, J., dissenting).

compound was produced that had no known benefit to society.[153] Fisher's ESTs on the other hand, had a beneficial use to society. First, they could help to reveal the underlying sequence of the protein that is encoded by the EST's corresponding DNA, and therefore help in understanding the genome of the maize plant.[154] And second, the ESTs could be used effectively as probes to see if a certain tissue expressed the mRNA corresponding to the EST sequences.[155]

Further, Judge Rader analogized the ESTs to a microscope, which had utility under 35 U.S.C. § 101.[156] First, both help a researcher take "one step closer to identifying and understanding a previously unknown and invisible structure."[157] Second, both reveal molecular structural information.[158] Third, both can "unlock[] the secrets of the corn genome to provide better food production for the hungry world." [159]

Judge Rader further accused the majority of being "oblivious to the challenges of complex research," and concluding with "little scientific foundation" that the claimed ESTs would not produce an immediate scientific benefit, or have assurances of being useful in the future.[160] He noted that only "the final step of a lengthy incremental research inquiry gets protection" if tools are only patentable when further research is not required, if the majority's holding is to be law.[161] He noted that in a recent publication in the scientific journal, *Nature*, that ESTs have been successfully shown to have utility through aiding the identification of genes involved in breast cancer cell metastasis from the primary breast tumor to a secondary tumor on the lung.[162] Similarly, he noted, a microscope helps a pathologist to determine the difference between normal tissue and tissue that is cancerous or malignant, but doesn't tell the researcher what the underlying cause of the malignancy is.[163] In the same manner, an EST sheds light on the underlying gene's sequence, but not its function.

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153. *Id.* at 1380 (Rader, J., dissenting).

154. *Id.*

155. *Id.*

156. *Id.*

157. *Id.*

158. *Fisher*, 421 F.3d at 1379 (Rader, J., dissenting).

159. *Id.*

160. *Id.*

161. *Id.*

162. *Id.* at 1381 n.1 (citing research from Andy J. Minn et al., *Genes that Mediate Breast Cancer Metastasis to Lung*, 436 NATURE 518 (2005)).

163. *See id.* at 1380-81.

III. THE LEGAL PROBLEM

Although the *Fisher* case produced a two-to-one majority decision, questions still remain concerning the heightened utility requirement and the patentability of ESTs as inventions. The last time that the Supreme Court has ruled on utility was in 1966 in *Brenner* where it held that certain inventions must have both substantial and specific utility.[164] The Court declined to delineate the test for both types of utility,[165] and the CAFC has subsequently been required to define these tests for utility as new technology arises as they did in *Fisher*.

In light of the lack of a specific test for the Supreme Court's heightened standard, combined with the fact that more and more biological subject matter will be presented to both the USPTO and the CAFC, some have questioned whose reasoning in *Fisher* will be followed by future courts—Judge Rader's, or the majority's?[166] Furthermore, if such a case were to reach the Supreme Court, would Judge Rader's dissent persuade the Court?

Additionally, the question has been raised as to whether or not ESTs are completely unpatentable after *Fisher*, or if the court left room for certain patentable utilities. Surely the majority did not say outright that ESTs are unpatentable, but only that Fisher did not present enough evidence that their patent application presented a substantial or specific use for the 5 selected ESTs. Naturally, the question to be asked is: what does one have to do in order to find a substantial and specific utility and obtain patent protection on a novel EST?

IV. ANALYSIS AND PROPOSAL

The following section suggests that Judge Rader's dissent, though thoughtful, is flawed. This section also proposes specific types of uses for ESTs that may meet the heightened utility requirement.

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164. MUELLER, *supra* note 23, at 159.

165. *See generally* Brenner v. Manson, 383 U.S. 519 (1966) (mentioning no standards through which a determination of both substantial and specific utility may be made). In fact, the USPTO issued guidelines in 2001 to address the utility standards set forth in *Brenner*. MUELLER, *supra* note 23, at 160.

166. Jones *supra* note 1, at 11.

A. The Dissent from Judge Rader Should Not Be Followed in Subsequent Rulings

In the event either that future courts or even the Supreme Court on appeal should have to address the issue of the utility requirement in EST patent applications, Judge Rader's dissent in *Fisher* should not be followed. Although he presented a detailed and spirited dissent in favor of granting utility to Fisher's ESTs, the central analogy he drew is misguided. The comparison of an EST to a microscope contains some serious flaws.

First, microscopes are patentable and useful by providing a means to examine almost limitless information about biological structures never seen previously by the naked eye.[167] Judge Rader is generally correct when he states that both an EST and a microscope "supply information about a molecular structure,"[168] but upon deeper scrutiny the analogy falters. An EST generally supplies information about *one* molecular structure—its underlying gene. A microscope however reveals information about *many* molecular structures. Analyzing many molecular or biological structures would certainly produce data that immediately and significantly add to biological knowledge without the need for further experimentation, unlike ESTs. Therefore, this invention would produce a presently available benefit to the public, satisfying the substantial utility requirement of *Fisher* and *Brenner*. Further, a microscope produces knowledge that is not vague, but provides specific data on various biological phenomena including biological structures, satisfying the specific utility requirement.

In contrast, an EST is a partial sequence of one gene.[169] Although it may be capable of analyzing biological phenomena like a research tool as Judge Rader suggests,[170] the substance of that phenomena is one gene, not the myriad biological structures capable of being examined through a microscope. There is no assurance that the gene in question will be important in disease or have any other useful medical application. Thus there is no certainty of producing a presently available benefit to the public as required by the substantial utility requirement. Additionally, because the utility of that

167. *See, e.g.*, U.S. Patent No. 6,987,609 (filed Sept. 4, 2002) (granting a patent for an improved microscope).

168. *Fisher*, 421 F.3d at 1380 (Rader, J., dissenting).

169. *See* discussion *supra* Section II.B.

170. *Fisher*, 421 F.3d at 1379 (Rader, J., dissenting).

underlying gene is unknown and uncertain to produce meaningful data, it is vague, and the specific utility requirement is not satisfied.

Thus, a better comparison that can be made between a microscope and ESTs is to the general invention of the EST technology itself, not to any specific EST. Inventing the method of creating these thousands of express sequence tags that correspond to genes enables the molecular biologist to explore the vast realm of gene sequences in general.[171] Examining thousands of genes is sure to produce information with a substantial and presently available benefit to the public that is not vague or meaningless, much like examining the vast array of biological structures with a microscope.

B. *Possible Substantial and Specific Utilities in Light of* Brenner v. Manson *and Subsequent Cases*

Although *Fisher* did not find a substantial utility for the asserted claims, there are at least two conceivable uses for ESTs that may have both substantial and specific utility in a clinical setting. Both derive from claims in the Fisher patent application.[172] As for Fisher's other claims, they rely on further sequencing of the gene in either its regulatory regions or its full-length form, requiring a patent application on the full-length gene.[173] Therefore the two proposed utilities would be supported upon the disclosure of the EST sequence itself.

What must a patent applicant do in order to avoid the rejections faced in *Fisher*? The court in *Fisher* acknowledged that ESTs had similarities to the rejected chemical compounds of *Brenner* and *Kirk*.[174] Therefore, the path to reaching the utility threshold must lie in the subsequent cases such as *Jolles*[175] and *Cross*[176] where the courts found the applications for similar chemical compounds to have substantial and specific utility.

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171. One such technology is the method of rapidly producing RNA and sequencing corresponding ESTs utilized by Dr. J. Craig Venter and his NIH colleagues to produce the first large EST patent application in 1992. *See* Holman & Munzer, *supra* note 5, at 750.

172. *Fisher*, 421 F.3d at 1368.

173. *See id.* at 1376 (stating that allowing a patent would just lead to a search to gain information about the underlying genes and proteins).

174. *See id.* at 1374-75.

175. *In re* Jolles, 628 F.2d 1322 (C.C.P.A. 1980).

176. Cross v. Iizuka, 753 F.2d 1040 (Fed. Cir. 1985).

C. *Single Nucleotide Polymorphisms Derived from ESTs*

The first possible use that an EST may possess stems from Fisher's fourth asserted claim addressing the subject matter of SNPs. The court in *Fisher* noted that Fisher had not identified any polymorphism nor presented any evidence that it would have a specific and substantial.[177] This is akin to claiming a general and nebulous utility to "biological activity" for the chemical compounds in *Kirk*.[178] Despite later filing an affidavit revealing specific biological activity of the compounds after the date of filing the patent application, the claims failed because of lack of support in the patent application at the time of filing.[179]

Therefore, an inventor applying for patent protection for SNP utilities using ESTs must employ the successful strategies used in the patent applications of *Jolles* and *Cross*. If a claim relating to a SNP revealed on an EST sequence is to pass the utility threshold, the first step is to include information in the patent specification that provides the SNP. For example, one should include the more predominantly-expressed sequence of the EST as well as the sequence of the EST with the SNP variation. Additionally, one should specifically note the variation in sequence between populations of that species. However, predicting the effect of the SNP on the biology of an organism and entering that prediction into the specification would likely be significantly more difficult than predicting the anti-cancer effects of the naphthacene compounds in the specification in *Jolles*. Therefore, more work would be required.

The second step towards reaching the utility threshold would be to correlate the occurrence of the SNP to either a disease or some other biological trait. In the same vein, correlating a SNP to a population that responds differently to specific drug treatments would work as well. The data that would be required would demand substantially more research than that disclosed in Fisher's application, and would encompassing the genotyping[180] of the specific

177. *Fisher*, 421 F.3d at 1373 ("Fisher does not present either a single polymorphism or a single promoter, assuming at least one of each exists, actually identified by using the claimed ESTs. Further, Fisher has not shown that a polymorphism or promoter so identified would have a 'specific and substantial' use.").

178. *Id.* at 1371.

179. *In re* Kirk, 376 F.2d 936, 941 (C.C.P.A. 1967).

180. Genotyping is the determining the frequency of an allele (in this case, frequency of a SNP) in a population. *See* OXFORD DICTIONARY OF BIOLOGY, *supra* note 26, at 277 (defining genotype frequency).

polymorphism, but it also would not produce a patent application surely to be rejected for failing the utility test.

Producing data to link a SNP to a specific trait of certain subpopulations of a species compares nicely with the data presented in *Jolles* and *Cross*. In both cases, *in vitro* and *in vivo* data was presented, and supported the respective claims of anti-tumorigenicity and thromboxane synthetase.[181] Similarly, a genotyping study performed to prove the association of a SNP with a specific biological trait is an *in vitro* study with immediate *in vivo* effects. It would allow the production of a possible diagnostic test to detect the trait. Indeed, such tests have been the focus of commercialization before.[182]

Therefore, producing this detailed, but essential data should allow for an EST to pass the utility threshold. Correlating a SNP to a biological trait through genotyping and statistical analysis should provide a "significant and substantial benefit to the public", particularly if it can help to predict populations at risk for disease that may respond to drug treatment differently than the general population. Additionally, identifying the link between a specific biological trait and a SNP would not be "so vague as to be meaningless," and provide for specific utility.

D. Use of ESTs as Probes for Gene Expression

Another way in which an EST could pass the utility threshold is by using it as a probe in gene expression studies, such as with microarrays. This stems also from one of Fisher's claims, "measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression."[183] This was Fisher's second claim, and was dropped by the time it reached the CAFC.[184] However, through correctly applying the successful techniques used in *Jolles* and *Cross*, it should produce a valid utility for an EST.

Like elucidating the role of a SNP, using an EST as a probe for a microarray would entail significant experimentation that would be included in the patent application. Generally, the ESTs of interest must be placed onto the surface of a slide or a bead, and involve a labeling system to detect expression levels of the EST.[185] mRNA from

181. *See* discussion *supra* Section II.F.

182. Roger Coronini et al., *Decoding the Literature on Genetic Variation*, 21 NATURE BIOTECHNOLOGY 21 (2003).

183. *Fisher*, 421 F.3d at 1368.

184. *Id.*

185. *See* discussion *supra* Section II.D.

different tissues, such from a breast cancer tumor and normal, non-diseased breast tissue would be screened with the EST-linked slide or bead, and relative levels of expression of the EST recorded in each tissue. If the EST's expression level is found to correlate either negatively or positively with a disease state, then a specific link to the disease may have been found.

This correlation, derived from *in vitro* experimentation as in *Jolles* and *Cross* would play a substantial role in detecting tissue suspected of being diseased, as with cancer. The EST would have utility as a probe to detect the levels of its corresponding gene's expression in that diseased tissue. And the important *in vitro* data would be the "first link in the screening chain" mentioned in *Fujikawa*, with reasonable correlation to what is occurring *in vivo*.[186] Thus the EST itself, without the entire underlying gene sequence would provide a specific and particular benefit to the public in the form of a diagnostic kit, as required under the substantial utility test. And as with SNP detection, data listed in the specification about the specific correlation to disease would provide a specific utility without the vagueness found by the court in *Fisher*.[187]

E. Policy Considerations of Allowing These Claims on ESTs

The delaying of scientific discovery and discouraging of scientific research was seen as the most important policy implication in *Fisher*.[188] It was feared that granting patents on an EST when the EST had not passed the utility requirement, would block others from researching the underlying gene and create a complicated environment for licensing.[189]

This proposal, in allowing some claims to ESTs, addresses that issue by focusing on the precise utilities that the EST can possess, and requiring significant research to be included in the patent application before the utility threshold is met. An inventor would be allowed claims to use the EST for specific functions such as screening for a specific trait, disease, or response to pharmacological treatment. These uses preclude competitors from using the EST sequence itself for screening those specific traits, but not for researching the gene if it were involved in another, unclaimed and un-researched application. Furthermore, as discussed above, claims to the underlying gene of an

186. *See* discussion *supra* Section II.F.

187. *See* discussion *supra* Section II.G.

188. *Fisher*, 421 F.3d at 1378.

189. *See id.*

EST would not meet the utility requirement, allowing for its further unimpeded study.

V. CONCLUSION

Despite some reports to the contrary, the *Fisher* ruling did not signal the death of patent applications for expressed sequence tags. The *Fisher* court found reason to apply the substantial and specific utility requirement employed previously for chemical compounds by the Supreme Court, to these short DNA sequences. In ruling that Fisher's ESTs did not reach the utility threshold, it defined substantial utility as having "a significant and presently available benefit to the public," and specific utility as having a "use which is not so vague as to be meaningless."[190] Although Fisher's specification did not support its proposed uses, it is evident that cases subsequent to *Brenner* reveal how ESTs might have some legal utility. Through production of data correlating biological traits to either SNPs in the expressed sequence tags, or to mRNA expression levels of ESTs, inventors may salvage substantial and specific utility out of ESTs. And by focusing on correlating biological traits to ESTs, and not allowing for broad claims encompassing the entire underlying gene, policy concerns about impeding scientific progress are adequately addressed.

190. *Id.* at 1371. *See also* discussion *supra* Section II.G.